REMARKS

Claims 11 –30 are pending. Claim 1 has been amended to replace "combination" with "reaction system" and to clarify the language. Support for the amendment can be found at least in page 4, lines 26-30 of the specification. Claim 22 has been amended to replace "the aromatic hydrocarbon is" with "the organic phase comprises." Support for the amendment can be found at least in page 3, lines 14-16 of the specification.

No new matter has been added. Upon entry of this amendment, claims 11 – 30 will be pending.

Claim Rejections – 35 USC §112

Claims 11 – 14, 19 – 21, 22, 25, and 27 – 30 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants traverse the rejections.

Specifically, the Office Action contends that it is unclear how the combination is maintained at the temperature range. Applicants point out that, based on the description in page 4, lines 26-30 of the specification, one of ordinary skill in the art would have understood that maintaining the combination at a temperature range means maintaining the reaction system at a temperature range. However, to advance prosecution, Applicants have replaced "combination" with "reaction system" in claim 1 and further amended claim 1 to clarify the language.

The Office Action also contends that claim 22 lacks antecedent basis from claim 21. Applicants point out that original claim 22 refers to the aromatic hydrocarbon recited in claim 21. However, to advance prosecution, Applicants have amended claim 22 to be dependent from claim 11.

For at least the reasons stated above, withdrawal of the rejections is respectfully requested.

Claim Rejections – 35 USC §103 over Bernhart in view of Anderson, Cuadro, and Alvarez-Builla

Claims 11 – 30 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over US Patent No. 5,270,317 ("Bernhart") in view of International Patent Publication No. WO99/38847 ("Anderson"), Cuadro, A.M. et al, "Synthesis of N-(Aminoethyl)azoles under Phase Transfer Catalysis," *Synthetic Communications*, 21(4), 535-544, 1991 ("Cuadro") and Alvarez-Builla J. et al, "1,5-Bis-(N-Benzyl-N,N-Diethylammonium) Diethylether, Dichloride (BBDE Cl). A Novel Bis-Ammonium Salt as Phase Transfer Catalyst," *Tetrahedron*, Vol. 46 (3), 967-978, 1990 ("Alvarez-Builla"). Applicants traverse the rejections.

The Office Action admits that Bernhart does not teach the use of a phase transfer catalyst and that none of Anderson, Cuadro, and Alvarez-Builla teaches the making of 2-butyl-3-[2'-(triphenylmethyl tetrazol-5-yl)-biphenyl-4-ylmethyl]-1,3-diazaspiro[4.4]non-1-ene-4-one ("IRB-03"). However, the Office Action contends that it would have been obvious to replace the 5-(4'-bromomethyl[1,1'-biphenyl]-2-carbonitrile disclosed in Anderson with 5-(4'-bromomethylbiphenyl-2-yl)-1-trityl-1H-tetrazole ("IRB-02") to reach the presently-claimed invention. Applicants respectfully disagree because there would have been no reasonable expectation of success.

Anderson discloses the N-alkylation of a 2-R-1,3-diazaspiro[4.4]nonan-4-one hydrochloride by reacting with a 4'-(halomethyl)[1,1'-biphenyl]-2-carbonitrile, such as 5-(4'-bromomethyl[1,1'-biphenyl]-2-carbonitrile, under phase-transfer catalysis conditions, which include the presence of an aqueous solution of standard inorganic bases. See Anderson, page 6, lines 12-21 and Examples 2 and 3. The N-alkylation is therefore conducted under a basic environment[1]. If the cyano group in 5-(4'-bromomethyl[1,1'-biphenyl]-2-carbonitrile was replaced with a trityl protected tetrazole group, however, one of ordinary skill in the art would have expected that the trityl group be removed under the basic environment because it is known in the art that trityl group can be removed under basic or acidic conditions. Such a removal would lead to the internal alkylation between the bromine and the tetrazole group rather than the desired N-alkylation of the spiro group. Therefore, there would have been no reasonable expectation of success to produce IRB-03 using IRB-02 as a starting material under the phase-

[1] Cuadro and Alvarez-Builla also disclose phase-transfer catalysis under basic environment only. See Cuadro, page 540, 1st paragraph; Alvarez-Builla, page 974, last paragraph.

transfer catalysis conditions disclosed in Anderson. Consequently, one of ordinary skill in the art would not have been motivated to substitute the cyano group in Anderson's 5-(4'-bromomethyl[1,1'-biphenyl]-2-carbonitrile with a trityl protected tetrazole group or to combine Anderson and Bernhart in general. Applicants, on the other hand, have found, surprisingly, that the removal of trityl group from the tetrazole group did not occur even under a basic condition in a phase transfer reaction, and therefore found that IRB-02 could react with 2-butyl-1,3-diaza-spiro[4.4]non-1-ene-4-one in the presence of a phase transfer catalyst as recited in the claims.

For at least the reasons stated above, a *prima facie* case of obviousness has not been established. Withdrawal of the rejections is respectfully requested.

CONCLUSION

Applicants submit that the claims are allowable. An early and favorable action to that effect is respectfully requested.

The Examiner is invited to contact the undersigned to discuss any issues regarding this response.

In the event that the filing of this paper is deemed not timely, applicants petition for an appropriate extension of time. The Office is authorized to charge any underpayment or credit any overpayment to Kenyon & Kenyon LLP's Deposit Account No. 11-0600.

Respectfully submitted,
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